Tabelle II. Die Wirkung des β-adrenergen Rezeptoren-Hemmers LB 46 (Visken) bei Verabreichung verschiedener Strahlenschutzsubstanzen vor Röntgenbestrahlung von männlichen Mäusen

Substanz	Rezeptoren-Hemmer	Strahlendosis R	Überlebende Tiere ohne Rez.-Block (%)	Überlebende Tiere mit Rez.-Block. (%)	P
AET	LB 46 (Visken)	1120	50,0	8,0	$<0{,}001$
Cystamin		1120	66,0	37,0	<0.01
Serotonin		1050	56,0	42,0	$>0{,}5$
TACE		810	54,0	2,0	$<0{,}001$
LPS*		810	59,6	44,0	$<0{,}01$

* Weibliche Tiere

1120 R, d.h. jeweils mit einer Strahlendosis, die bei den mit der entsprechenden Schutzsubstanz behandelten Tieren 30 Tage p.rad eine Überlebensrate zwischen 50 und 70% ergab. Die einzelnen Versuchsgruppen bestanden stets aus 50 Tieren. Ausserdem wurden 300 unbehandelte Mäuse mit 750 R zur Festlegung des Kontrollwertes für unbehandelte Mäuse (1. Versuch) bestrahlt. Ihre Überlebensrate betrug 30 Tage p.rad 21,0%.

Die Resultate unserer Versuche sind in den Tabellen I und II dargestellt. Wie aus den in den Tabellen wiedergegebenen Resultaten geschlossen werden kann, wird bei einer zusätzlichen Verabreichung von β-adrenergen Rezeptoren-Hemmstoffen die Überlebensrate von bestrahlten geschützten Mäusen signifikant herabgesetzt ($P <$ 0,01–0,001). Eine Ausnahme hiervon bildet lediglich das Resultat bei den mit Serotonin vorbehandelten Versuchstieren. Dieser Befund dürfte jedoch damit zu erklären sein, dass Serotonin nicht mit β-adrenergen, sondern mit serotonin-spezifischen Rezeptoren eine Komplexbindung eingeht. Die Wirksamkeit des Regitins (Phentolamin) als einem α-adrenergen Rezeptoren-Hemmer deutet darauf hin, dass das Phentolamin in unserem Falle in der Lage ist, auch die β-adrenergen Rezeptoren hemmend zu beeinflussen, d.h. dass es sich bei dem Regitin nicht um einen α-adrenergen Blocker hoher Spezifität in dem Sinne handelt, wie dies für das Visken (LB 46) als β-adrenergen Rezeptoren-Hemmer gilt.

Aus unseren Ergebnissen folgern wir[3,4] weiterhin, dass die von uns verwendeten Schutzsubstanzen zu der Gruppe derjenigen chemischen Stoffe gehören, die das membrangebundene Adenyl-cyclase-System stimulieren, die Konzentration des cAMP in den Effektor-Zellen steigern und dadurch die Strahlenresistenz eines Organismus erhöhen.

Summary. The effect of β-adrenergic receptor-inhibitors was examined in relation to the effectiveness of radioprotective agents. The results, when mice were irradiated, show that the receptor-inhibitors significantly reduced the effect of the applied protectors.

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Some Pharmacological Properties of Oxytocin-Dimers ($\alpha+\beta$)

The final step in the synthesis of oxytocin[1,2] is the cyclisation of the linear disulphhydryl intermediate, oxytocein, by oxidation. This reaction, however, also results to a certain extent in the formation of a compound, oxytocin-dimer, which consists of two straight chain oxytocein molecules linked together by two disulphide bridges.

The structures of the two possible oxytocin-dimers, the parallel isomer and the antiparallel isomer, are depicted in the Figure. Indeed the oxytocin-dimer generated in oxytocin synthesis, although it behaves as a single compound in partition chromatography on Sephadex G25, is a mixture of these two isomers as shown by YAMASHIRO, HOPE and DU VIGNEAU[3]. The parallel dimer was recently synthetized by AANNING and YAMASHIRO[4] and shown to be identical with the α-dimer of YAMASHIRO, HOPE and DU VIGNEAUD.

Since synthetic oxytocin containing oxytocin-dimers ($\alpha + \beta$) is clinically used, it seems of general interest to assess the main biological activities of the mixture of these error peptides (dimers $\alpha + \beta$).

The oxytocin-dimers ($\alpha + \beta$) were isolated from crude synthetic oxytocin by countercurrent distribution in the following system: sec. butanol-water-acetic acid (1000: 1200:1). After 200 transfers a separation into 2 peaks with K values of 0.25 and 0.39 had been accomplished as detected by the Folin-LOWRY color reaction[5]. The material of the major peak ($K = 0.39$) proved to be pure oxytocin whereas the slower moving material of the second sharp symmetric peak ($K = 0.25$) represents, to all probability, the oxytocin-dimers. An acid hydrolysate of the material had an amino acid composition identical with that of an hydrolysate of oxytocin. But the material exhibited very low biological activity.

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Pharmacological activities in IU per mg

Compound	Oxytocin-like activities				Vasopressin-like activities	
	Rat uterus (in vitro)	Cat uterus (in situ)	Rabbit mammary gland (in situ)	Chicken blood pressure	Rat blood pressure	Rat antidiuresis
	1	2	3	4	5	6
(A) Oxytocin-dimers ($\alpha+\beta$)	3.0 ± 0.15	15.4[a]	3.7[a]	3.1[a]	0.044 ± 0.003	0.02 ± 0.0025
Oxytocin-dimer[b]						
α = parallel	1	—	—	—	—	—
β = antiparallel	1	—	—	—	—	—
(B) Oxytocin[c]	450 ± 30	450	450 ± 30	450 ± 30	5 ± 1	5 ± 1
A:B	0.007	0.034	0.008	0.007	0.009	0.004

[a] Approximations calculated from dose-response-lines as substance interferes with usual test procedure. [b] According to YAMASHIRO, HOPE and DU VIGNEAUD[3]. [c] According to BERDE and BOISSONNAS[6]. 1. HOLTON[7]; 2. BERDE, DOEPFER and KONZETT[8]; 3. BERDE and CERLETTI[9]; 4. U.S.P. XIV[10]; 5. British Pharmacopeia[11]; 6. BERDE and CERLETTI[12].

The biological activity of the oxytocin-dimers ($\alpha + \beta$) was determined in the usual tests, and the results are summarized in the Table. For comparison, the published activities of the oxytocin-dimers α and β and corresponding potencies of oxytocin are also included.

The oxytocin-dimers ($\alpha + \beta$) showed very low but definite oxytocin- and vasopressin-like activities. The result on the isolated rat uterus is similar to previous findings. Compared with oxytocin, the relative activity (A:B) is of the order of 1% on a weight basis and 2% on a molar-basis respectively with one exception: the cat uterus in situ where it reaches 3.4% (w/w) and 6.8% (mol/mol) respectively. In the rat preparations there were practically no qualitative differences between the pharmacological effects of equipotent doses of oxytocin and oxytocin-dimers ($\alpha + \beta$). However, in the experiments using cats, rabbits and chickens, differences in time course and moreover influences on the reactions to subsequent injections of oxytocin have been observed. Oxytocin-dimers ($\alpha + \beta$) are less toxic than oxytocin when administered i.v. to rats. The acute LD_{50} is 43 mg/kg (oxytocin: 25 mg/kg).

Zusammenfassung. Oxytocin-Dimer ($\alpha + \beta$), ein Nebenprodukt der Oxytocin-Synthese, zeigt in 6 Versuchsanordnungen schwache, aber messbare neurohypophysäre Aktivitäten.

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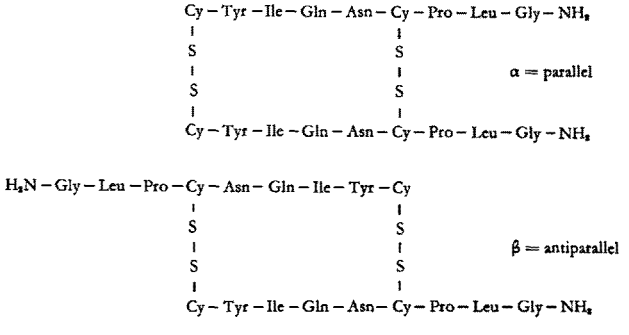
Oxytocin-dimers



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A Comparative Study of Inulin and Sodium Sulfanilate Clearances in Sheep and Goats

Considerable research has been conducted on the problem of glomerular filtration rate (GFR)[1,2] and the mechanism of tubular transport of several substances present in the glomerular filtration or in the blood plasma which perfuses the tubules[3–5]. The concept of 'clearance' has been generalized for all aspects of renal excretion and includes filtration, tubular secretion and absorption. During the decade of 1925–1935 several investigators found different substances that have the ability of being transported[6–8] and concentrated by kidney in a larger amount than their plasma concentration; creatinine for instance shows that property in some species.

The introduction of inulin for the measurement of glomerular filtration rate made it possible to study the physiology of the tubules. Tubular activity can easily be shown by comparison of the clearances of substances which are secreted or reabsorbed by the tubules with that of inulin[9,10]. If a substance has a higher clearance than inulin, the substance must have been added to the filtrate by secretion of the tubules; conversely if substances which have been filtered do not appear in the urine or have clear ance rates less than that of inulin the substances must have been removed from the filtrate by the tubules. Examples of the former mechanism are the clearance of